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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,355	04/28/2005	Ulrich Schubert	208244/0002	8343

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
06/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,355	SCHUBERT ET AL.	
	Examiner	Art Unit	
	ABDEL A. MOHAMED	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-86* is/are pending in the application.

4a) Of the above claim(s) *54-86* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 April 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/13/06,10/5/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

REASSIGNMENT AFFECTING APPLICATION LOCATION

1. The Group and/or Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1654.

ACKNOWLEDGEMENT FOR PRIORITY, IDS, AMENDMENT, RESPONSE TO RESTRICTION REQUIREMENT, STATUS OF THE APPLICATION AND CLAIMS

2. This application is application is filed under 35 U.S.C. 371 on 04/28/05 having a filing date of 04/04/03 of PCT/DE03/01213. Acknowledgement is made of Applicant's claim of priority based on German Application Number 102 16 227.1 having a filing date of 04/05/02. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119, which papers have been placed of record in the file. The information disclosure statements (IDS) and Form PTO-1449 filed 10/05/04 and 04/13/06, the amendment filed 01/10/06 and response to the restriction requirement filed 11/27/07, respectively are acknowledged, entered and considered. In view of Applicant's request claims 1-43 have been canceled and claims 44, 45, 54-60 and 72-86 have been amended. Claims 44-86 are now pending in the application.

CLAIMS STAND WITHDRAWN WITHOUT TRAVERSE

3. Applicant's election of Group I, (claims 44-53) in response filed 11/27/07 is acknowledged. Although, Applicant has elected to prosecute the invention of Group I without traverse; however, Applicant further elected Species within Group I for the purpose of prosecution. Nevertheless, Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election **without** traverse (MPEP § 818.03(a)). Applicant has elected the following species within Group I:

Claim 44: Flavivirus;

Claim 45: Falvivirus-induced fever;

Claims 46-48: Inhibits the activities of the ubiquitin/proteasome pathway;

Claims 51-53: the boric acid derivatives of modified peptide aldehydes.

Therefore, all the other non-elected species within Group I and the inventions of Groups II and III (i.e., claims 54-86) are withdrawn. The Office action is directed to the merits of claims of Group I of claims 44-53 along the above elected species within claims 44-53 as per elected invention and species and claims 54-86 are withdrawn as non-elected inventions.

OBJECTIONTO THE SPECIFICATION

4. The specification is objected to because the priority data of this application should be updated in the specification. Appropriate correction is required. Further, the disclosure is objected because of the following informalities: Figures 3, 6, 9 and 10 have

multiple figures. The figures should be amended in the instant specification to read Figures 3A and 3B; Figures 6A and 6B; Figures 9A, 9B and 9C; and Figures 10A and 10B, respectively. Thus, appropriate correction is required. Also, the disclosure is objected to of the following informalities: For example, page 10, the last two lines and page 11, the first three lines, contain an embedded hyperlink directed to an Internet addresses. The use of hyperlinks and/or other form of browser-executable code is not permitted under USPTO current policy because the content of such links are subject to a change, resulting in the introduction of New Matter into the specification. Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

CLAIMS REJECTION-35 U.S.C. § 102(e)

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 44-53 are rejected under 35 U.S.C. 102(e) as being anticipated by Schubert et al (Pub. No. US 2004/0106539 A1) Cited by Applicant on IDS filed 4/13/06.

The elected claims are drawn to an agent for inhibiting at least one of release, maturation and replication of a member of the *Flavivirdae* family selected from *Flavivirus* wherein the agent comprises, as an active component, at least one proteasome inhibitor in a pharmaceutical preparation (claim 44), wherein the agent is used for the treatment and prophylaxis of HCV-induced hepatitis, falvivirus-induced fever (claim 45), wherein the proteasome inhibitor is a substance which affects the activities of the ubiquitin/proteasome pathway; which specifically affects the enzymatic activities of the complete 26S proteasome complex; and which specifically affects the enzymatic activities of the free 20S catalytically active, proteasome complex, which is not assembled with regulatory subunits (claim 46), wherein the proteasome inhibitor is taken up by higher eukaryotic cells and, after having been taken up into a cell, interacts with the catalytic subunits of the proteasome, and, in connection with this, blocks at least some of the proteolytic activities of the proteasome within the 26S or the 20S proteasome complex (claim 47), wherein in addition to proteasome inhibitors, the pharmaceutical preparation also comprises at least one further agent which inhibits the cellular ubiquitin system, such as the activities of the ubiquitin-conjugating enzymes and/or of the ubiquitin-hydrolyzing enzymes (claim 48), wherein the proteasome inhibitor is administered in various mode of administrations as recited in claim 49, wherein the proteasome inhibitor is produced from various sources as recited in claim 50, the boric acid derivatives of modifies aldehydes (claim 51), epoxomycin (claim 52) and PS-341 (claim 53).

The reference of Schubert et al ('539) discloses agents for the treatment of viral infections, in particular, infections with hepatitis of acute and chronic HCV such as Flavivirus. Said agents inhibit the release, maturation and replication of hepatitis virus among others viruses. In the example, hepatitis virus has been shown that the proteasome inhibitors (i.e., active component of the claimed invention) block the release of virus particles and the infectiousness of the released viral particles and thus the production of the viruses. The proteasome inhibitors affect the activities of the ubiquitin/proteasome pathway, in particular the enzymatic activities of the 26S and 20S proteasome complexes (See e.g., abstract, ¶ 0002, 0005, 0006 and particularly 0060).

The '539 discloses a composition comprising a proteasome inhibitor and a pharmaceutically acceptable carrier, wherein the proteasome inhibitor is a boric acid derivative. The inhibitor of '539 contains a boric acid radical, specifically dipeptidyl boric acid derivatives, more specifically the compound pyranosyl-phenyl-leucinyl-boric acid, referred to as "PS-341". This is further evidenced by Applicant's disclosure in the instant specification on ¶ 0011 by stating another, and very potent, class of synthetic proteasome inhibitors are boric acid peptide derivatives, in particular the compound pyranosyl-phenyl-leucinyl-boric acid, which is named "PS-341". PS-341 is very stable under physiological conditions and is bio-available following intravenous administration.

The proteasome inhibitors of '539 is a synthetic substance. Additionally, the composition of the reference's is in a formulation that is suitable for various mode of administrations such as for oral, intravenous, intramuscular, subcutaneous, etc. (See e.g., ¶ 0076 and claim 6). Further, the '539 notes that the composition blocks peptide-

hydrolyzing activity within 26S or 20S proteasome complexes (See e.g., ¶ 0073). Additionally, as a proteasome inhibitor, the composition of '539 would necessarily inhibits, regulates or affects a ubiquitin proteasome pathway; affects enzymatic activity of a complete, 26S proteasome complex, or a free, catalytically active 20S proteasome structure not assembled with a regulatory subunit; and be taken up by eukaryotic cells and interacts with a catalytic proteasome subunit for all those properties are inherent of proteasome inhibitors (See e.g., ¶ 0072-0079, 0082, 0084, 0087 and 0091-0092).

It is noted that independent claim 44 is directed to a pharmaceutical formulation and claim 45 depends from claim 44, however, claim 45 (and dependent claims thereof i.e. claims 46-53) contain an intended use recitation "used for the treatment and prophylaxis of HCV-induced hepatitis, flavivirus-induced fever", the cited reference above does not disclose the intended use of the product/composition for the treatment of flavivirus-induced fever, although, the preamble of claim 1 of '539 states a composition for treating viral infection, characterized in that it contains at least one proteasome inhibitor as active component and in claim 32 the use of proteasome inhibitors for treating/controlling/preventing HCV-induced liver carcinomas and in claim 33 for HCV infection which may encompass the claimed falvivirus-induced fever; nevertheless a statement of usefulness or contemplated use of a claimed compound or composition in a claim is usually given little weight in distinguishing over the prior art. *In re Maeder et al.* (CCPA 1964) 337 F2d 875, 143 USPQ 248; *In re Riden et al.* (CCPA 1963) 318 F2d 761, 138 USPQ 112; *In re Sinex* (CCPA 1962) 309 F2d 488, 135 USPQ 302. Further, it is well established that the intended use of a compound (e.g., a

polypeptide or a protein or a glycoprotein) does not impart patentability to the compound. *In re Spada*, 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990) (The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition); *In re Pearson*, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition claims patentable); *In re Zierden*, 411 F.2d 1325, 1328, 162 USPQ 102, 104 (CCPA 1969).

Thus, sufficient evidence of similarity is deemed to be present between the instantly claimed invention of claims 44-53 and the prior art teachings which clearly discloses agents for the treatment and prophylaxis of viral infection which encompasses HCV-induced hepatitis, flavivirus-induce fever as disclosed in the abstract, ¶ 0002, 0005, 0016, 0060, 0071-0075, 00077-0079, 0082, 0087, 0091-0092 and claims 1-9, 11-14 and 32-34. Therefore, in the absence of evidence to the contrary or specific structural limitations, the claimed agents for treating flavivirus infections thereof as taught by the reference anticipates claims 44-53 as drafted.

CONCLUSION AND FUTURE CORRESPONDANCE

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABDEL A. MOHAMED whose telephone number is (571)272-0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mohamed/A. A. M./
Examiner, Art Unit 1654

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657